Based on the above amendments and the following Remarks, Applicants respectfully request that the Examiner reconsider and withdraw all outstanding rejections.

Rejections Under 35 U.S.C. § 102(b)

Claims 1, 22 and 23 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by "First Meeting of the WHO Alliance for the Global Elimination of Trachoma, Geneva, 30 June – 1 July 1997" (hereinafter "Dawson"). Dawson, however, is not a proper § 102(b) reference because it is not a "printed publication" and in addition because it is not enabling, and therefore cannot anticipate claims 1, 22 and 23.

It is Applicants' understanding that Dawson is a synopsis of an oral presentation given by Dr. Chandler Dawson, a named inventor of the present application, in Geneva, Switzerland at a private conference, and that Dawson was available only upon the request of the conference attendees. Dawson was not to Applicants' knowledge disseminated to the public or made publicly available before the priority date of the present application, *i.e.*, March 31, 1999.

The United States Court of Appeals for the Federal Circuit has stated that for a document to be considered a "printed publication" within the meaning of 35 U.S.C. §102(b), the "reference must have been sufficiently accessible to the public interested in the art; dissemination and public accessibility are the keys to the legal determination whether a prior art reference was 'published.'" *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1568 (Fed. Cir. 1988). Public accessibility "has been called the touchstone in determining whether a reference constitutes a 'printed publication' bar under 35 U.S.C. § 102(b)." *In Re Hall*, 781 F.2d 897, 899 (Fed. Cir. 1986).

Because Dawson was not disclosed publicly and was not otherwise available to the public before the critical date, Applicants contend that, in accordance with *In re Hall* and *Constant*, Dawson is unavailable as prior art under 35 U.S.C. § 102(b).

Further, even if Dawson is considered (incorrectly, Applicants believe) as prior art for the purposes of 35 U.S.C. § 102(b), Dawson is not an enabling disclosure, and as such, does not anticipate the claimed invention. Disclosures in publications must, through the "description and drawings contain and exhibit a substantial representation of the patented improvement, in such full, clear, and exact terms as to enable any person skilled in the art or science to which it appertains, to make, construct, and practice the invention to the same practical extent as they

would be enabled to do if the information was derived from a prior patent." *Seymour v. Osborne*, 78 U.S. 516, 555, 20 L. Ed. 33, 42, 11 Wall. 516 (1870). That is, the disclosure in a publication other than a patent must be enabling. *See In re Donohue*, 766 F.2d 531, 533 (Fed. Cir. 1985).

In order for Dawson to anticipate claims 1, 22, and 23, therefore, Dawson must adhere to the requirement in *Seymour* to provide an enabling disclosure. Regardless of any suggestions that Dawson appears to make, Dawson does not teach how to apply "an azalide antibiotic to an eye in an amount effective to treat or prevent infection in a tissue of the eye," as required by claim 1.

The Examiner asserts in the office action that Dawson, "suggest[s] the topical use of azithromycin to the treatment of an eye infection." (Examiner's Action, 4/14/2000, Page 3, emphasis added). Anticipation under 35 U.S.C. § 102(b) requires more than mere suggestion, however. Dawson not only does not suggest the claimed invention, it teaches that topical azithromycin was unavailable because it was not known how to make the compound: "[f]irst of all, a stable product must be developed." (Dawson, page 3). It is illogical to assert that Dawson provides an enabling disclosure concerning the application of an antibiotic when it clearly asserts that no product has been developed that comprises the antibiotic. Dawson also fails to teach how to use topical azithromycin, as evidenced by the query that "[i]f topical azithromycin becomes available, can it have a role in trachoma control programs?" (Dawson, page 3). As Dawson makes clear that no topical azithromycin was available at the time of the Dawson reference, Dawson cannot provide an enabling disclosure for purposes of anticipation of the method of application of a topical azithromycin such as in claim 1. Because Dawson is not an enabled reference for the purposes of 35 U.S.C. § 102(b), claims 1, 22, and 23 are not anticipated. In light of the above arguments, withdrawal of the 102(b) rejections is respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Claims 1-44 stand rejected under 35 U.S.C. § 103(a) as obvious over Bailey et al. (Lancet, vol. 342, pages 453-456 (1993), hereinafter "Bailey") in view of U.S. Patent No. 4,521,982 to Hauske et al. (hereinafter "Hauske") and further in view of WO 95/09601 to Kornman et al. (hereinafter, "Kornman"). Claims 30-35 have been cancelled without prejudice.

Claims 1-44 are not rendered obvious by the combination of Bailey with Hauske and Kornman, because while Bailey does teach oral administration of " . . . a single dose (20 mg/kg)

by mouth" of azithromycin for the treatment of trachoma (p. 454), Hauske and Kornman do not make the topical use of azithromycin obvious in light of Bailey. Hauske simply teaches that for topical application of the compound disclosed, "it will usually be convenient to prepare pharmaceutical compositions, in which the compound of formula III is combined with a pharmaceutically-acceptable carrier of diluent, for example in the form of ointments and creams." (Column 9, lines 24-29). Kornman teaches that, "Sustained release compositions are administered by gently placing the product in subgingival cavities of infected teeth." (p.8, lines 25-26).

Neither Bailey, nor Hauske, nor Kornman teaches or suggests the use of an antibiotic composition "topically . . . to an eye," which is a required element in each of claims 1-29. The MPEP instructs that, "[t]o establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)," and that "[a]ll words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wison*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970)." (MPEP § 2143.03). In the present case, the element of topical application to an eye is not present in any of the cited prior art, and claims 1-29 are not therefore obvious over Bailey in view of Hauske and Kornman.

Further, "[t]he mere fact that references <u>can</u> be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). The use of an oral antibiotic as taught in Bailey, and the separate use of that same antibiotic for topical application to non-eye areas as taught by Hauske and Kornman, with nothing else, does <u>not</u> suggest the use of the antibiotic topically in the eyes.

Claims 36-44 as well are not obvious over Bailey in view of Hauske and Kornman. Claims 36-44 are directed to suspensions (claims 36-39) and compositions (claims 40-44) comprising, *inter alia*, an azalide antibiotic and an additional medicament. According to *In Re Royka*, all of the claimed elements must be taught or suggested by the prior art references in order to establish prima facie obviousness. None of the cited references teach or suggest the use of additional medicaments in compositions comprising azalide antibiotics. Therefore, claims 36-44 are not obvious over Bailey in view of Hauske and Kornman.

a

Claims 30-44 stand rejected under 35 U.S.C. § 103(a) as obvious over Kornman. Claims 30-35 have been cancelled without prejudice. Claims 36-44 are not obvious over Kornman alone for the same reasons stated above for the 103(a) rejection of claims 36-44 over Bailey in view of Hauske and Kornman; Kornman does not teach or suggest the use of an additional medicament and does not therefore make claims 36-44 obvious under 35 U.S.C. 103 (a).

Claims 1-44 stand rejected under 35 U.S.C. 103(a) over Dawson in view of Kornman. Claims 30-35 have been cancelled without prejudice. Claims 1-29 are not obvious over Dawson in view of Kornman, however, because, as discussed above, Dawson is not an enabling disclosure for a composition comprising azalide antibiotics or a method for applying such a composition to an eye (as in claims 1-29), and Kornman does not remedy the defects present in Dawson. Specifically, Dawson teaches that, "the problems of antibiotic ointment for trachoma control are well known," and that azithromycin would need to be tested for "toxicity in the eye." (Dawson, page 3). It would not have been obvious to a person of ordinary skill in the art to combine Dawson, which is not an enabled disclosure, with Kornman, which discloses application of antibiotic to gum tissue and does not teach or suggest how to overcome the "problems" of application of antibiotic ointment to the eye noted in Dawson. The MPEP instructs that "[t]he prior art can be modified or combined . . . as long as there is a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986)." (MPEP § 2143.02). In the present case, a person with ordinary skill in the art would not expect success if the non-enabled disclosure of Dawson were combined with the orally applied antibiotics of Kornman, considering the differences in the tissue and application problems encountered.

Further, claims 36-44 comprise a suspension (claims 36-39) and a composition (claims 40-44), and Dawson adds nothing to the materials disclosed in Kornman concerning these elements. Claims 36-44 are directed to suspensions (claims 36-39) and compositions (claims 40-44) comprising, *inter alia*, an azalide antibiotic and an additional medicament. Neither Dawson nor Kornman appears to teach or suggest the use of additional medicaments in compositions or suspensions comprising azalide antibiotics, and, therefore under the rule of *In Re Royka*, claims 36-44 are not obvious over Dawson in view of Kornman.

In light of the above amendments and arguments, withdrawal of the 35 U.S.C. § 103(a) rejections is respectfully requested.

a

Rejections under 35 U.S.C. § 112, paragraph two

Claims 1-29 stand rejected under 35 U.S.C. § 112, paragraph two as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that, "it is not clear what is encompassed by the term 'prevent' (claim 1) i.e. it is not clear whether prevention is achieved for a period of days, months, years or whether permanent prevention is achieved." (Examiner's Action, Page 3).

The claims are not indefinite. Compliance with the definiteness requirement of 35 U.S.C. § 112, paragraph two, is a question of law that asks no more than if the claims, read in light of the specification, reasonably apprise those skilled in the art of the scope of the invention. *See Credle v. Bond*, 25 F.3d 1566, 1576, 30 U.S.Q.P.2d 1911, 1919 (Fed. Cir. 1994). The focus of the question revolves around a reasonable understanding of one of ordinary skill in the art. *See In re Miller*, 441 F.2d 689, 692-93, 169 U.S.P.Q. 597, 599 (C.C.P.A. 1971). MPEP § 2173.04 recites that the "[b]readth of a claim is not to be equated with indefiniteness." In the present case, the duration of prevention is not intended to limit the scope of claims 1-29. *See, e.g.*, claim 1, which recites: "[a] process for treating an eye, which comprises: topically applying an azalide antibiotic to an eye in an amount effective to treat or prevent infection in a tissue of the eye." A person of ordinary skill in the art will know or can determine without undue experimentation the duration of prevention, which will depend on the medical state of the animal being treated.

Further, "prevent" is unambiguously defined in the specification: " . . . treat or prevent infection in a tissue of the eye . . . means that the conditions of application result in a retarding or suppression of the infection." (Specification, p. 6) In light of the specification's clear definition, "prevent," as used in claims 1-29, is not indefinite, and, according to *Credle*, claims 1-29 are not indefinite under 35 U.S.C. § 112 paragraph two.

In light of the above arguments, the withdrawal of the rejections under 35 U.S.C. § 112 paragraph two is respectfully requested.

Conclusion

In view of the above, each of pending claims 1-29 and 36-44 in this application is believed to be in condition for immediate allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to

issue. The Examiner is invited to telephone the undersigned at (202) 383-7217 with respect to any unresolved issues remaining in this application.

Respectfully submitted,

Joel M. Freed (Reg. No. 25,101)
June E. Cohan (Reg. No. 43,741)
Andrew S. Brenc (Reg. No. 45,534)

Date: August 11, 2000

HOWREY SIMON ARNOLD & WHITE, LLP
1299 Pennsylvania Avenue, N.W.
Washington, D.C. 20004-2402
Attorneys for Applicant
Tel. (202) 383-7217
Fax (202) 383-6610